

DOCKET NO.: ISIS-2960 (ISIS0085-101)

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In the Claims:

The current status of all claims is listed below and supersedes all previous lists of claims.

Please amend claims 83, and 85-87 as follows:

1-82. (canceled).

83. (currently amended) A system of associated components for preparing a set of oligonucleotides that modulates expression of a selected nucleic acid comprising:

~~a computer system that prepares a virtual library of oligonucleotide sequences targeted to said selected nucleic acid and generates synthesis instructions in computer manipulable form for said oligonucleotide sequences in said virtual library, wherein said computer system first prepares said virtual library of oligonucleotide sequences and then reduces the number of oligonucleotide sequences in said virtual library of oligonucleotide sequences by a process of selection based on targeting a functional region of said selected nucleic acid;~~

i) generates a list of oligonucleotide sequences according to a desired oligonucleotide length, thereby generating a series of oligonucleotide sequences;

ii) applies a virtual oligonucleotide chemistry to the oligonucleotide sequences generated in step i) to yield a set of virtual oligonucleotides;

iii) generates a subset of said set of virtual oligonucleotides based on targeting a functional region of said selected nucleic acid; and

iv) generates synthesis instructions in computer manipulable form for said oligonucleotide sequences in said subset of said set of virtual oligonucleotides;

~~an automated synthesizer that receives said synthesis instructions from said computer system and synthesizes only that set of real oligonucleotides that corresponds to said virtual set of oligonucleotide sequences consisting of said reduced number of oligonucleotide sequences~~
said oligonucleotide sequences in said subset of said set of virtual oligonucleotides; and

~~an apparatus that accepts said set of real oligonucleotides and performs at least one procedure for each of said real oligonucleotides wherein said procedure identifies particular~~

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members of said set that modulate expression of said selected nucleic acid, ~~wherein said procedure is computer-controlled polymerase chain reaction or computer-controlled enzyme-linked immunosorbent assay.~~

84. (previously presented) The system of claim 83 wherein said functional region is the transcription start site, 5' cap, start codon, 5' untranslated region, 3' untranslated region, stop codon, 5' splice site or polyadenylation site.

85. (currently amended) A system of associated components for preparing a set of oligonucleotides that modulates expression of a selected nucleic acid comprising:

a computer system that ~~prepares a virtual library of oligonucleotide sequences targeted to said selected nucleic acid and generates synthesis instructions in computer-manipulable form for said oligonucleotide sequences in said virtual library, wherein said computer system first prepares said virtual library of oligonucleotide sequences and then reduces the number of oligonucleotide sequences in said virtual library of oligonucleotide sequences by one or more of~~ i) ~~a process of selection based on target accessibility to said selected nucleic acid, ii) a process of selection based on uniform distribution of oligonucleotide compounds across said selected nucleic acid, or iii) a process of selection based on targeting a functional region of said selected nucleic acid;~~

i) generates a list of oligonucleotide sequences according to a desired oligonucleotide length, thereby generating a series of oligonucleotide sequences;

ii) applies a virtual oligonucleotide chemistry to the oligonucleotide sequences generated in step i) to yield a set of virtual oligonucleotides;

iii) generates a subset of said set of virtual oligonucleotides based on: a) targeting a functional region of said selected nucleic acid, b) target accessibility to said selected nucleic acid, and/or c) uniform distribution of oligonucleotide compounds across said selected nucleic acid; and

iv) generates synthesis instructions in computer manipulable form for said oligonucleotide sequences in said subset of said set of virtual oligonucleotides;

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an automated synthesizer that receives said synthesis instructions from said computer system and synthesizes only ~~that set of real oligonucleotides that corresponds to said virtual set of oligonucleotide sequences consisting of said reduced number of oligonucleotide sequences~~ said oligonucleotide sequences in said subset of said set of virtual oligonucleotides;

a first apparatus that accepts said set of real oligonucleotides and performs at least one procedure for each of said real oligonucleotides wherein said procedure identifies particular members of said set that modulate expression of said selected nucleic acid, ~~wherein said procedure is computer-controlled polymerase chain reaction or computer-controlled enzyme-linked immunosorbent assay;~~ and

a second apparatus selected from the group consisting of liquid chromatography, optical density reader, mass spectroscopy, gel fluorescence and scintillation imaging, and capillary gel electrophoresis.

86. (currently amended) A system of associated components for preparing a set of oligonucleotides that modulates expression of a selected nucleic acid comprising:

a computer system that ~~prepares a virtual library of oligonucleotide sequences targeted to said selected nucleic acid and generates synthesis instructions in computer-manipulable form for said oligonucleotide sequences in said virtual library, wherein said computer system first prepares said virtual library of oligonucleotide sequences and then reduces the number of oligonucleotide sequences in said virtual library of oligonucleotides by one or more of i) a process of selection based on target accessibility to said selected nucleic acid, ii) a process of selection based on uniform distribution of oligonucleotide compounds across said selected nucleic acid, or iii) a process of selection based on targeting a functional region of said selected nucleic acid;~~

i) generates a list of oligonucleotide sequences according to a desired oligonucleotide length, thereby generating a series of oligonucleotide sequences;

ii) applies a virtual oligonucleotide chemistry to the oligonucleotide sequences generated in step i) to yield a set of virtual oligonucleotides;

iii) generates a subset of said set of virtual oligonucleotides based on: a) targeting a

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functional region of said selected nucleic acid, b) target accessibility to said selected nucleic acid, and/or c) uniform distribution of oligonucleotide compounds across said selected nucleic acid; and

iv) generates synthesis instructions in computer manipulable form for said oligonucleotide sequences in said subset of said set of virtual oligonucleotides;

~~an automated synthesizer that receives said synthesis instructions from said computer system and synthesizes only that set of real oligonucleotides that corresponds to said virtual set of oligonucleotide sequences consisting of said reduced number of oligonucleotide sequences~~
said oligonucleotide sequences in said subset of said set of virtual oligonucleotides; and

~~an apparatus that accepts said set of real oligonucleotides and performs at least one procedure for each of said real oligonucleotides wherein said procedure identifies particular members of said set that modulate expression of said selected nucleic acid, wherein said procedure is computer-controlled polymerase chain reaction or computer-controlled enzyme-linked immunosorbent assay; and wherein said property is modulating said selected nucleic acid.~~

87. (currently amended) A system of associated components for preparing a set of oligonucleotides that modulates expression of a selected nucleic acid comprising:

~~a computer system that prepares a virtual library of oligonucleotide sequences targeted to said selected nucleic acid and generates synthesis instructions in computer manipulable form for said oligonucleotide sequences in said virtual library, wherein said computer system first prepares said virtual library of oligonucleotide sequences and then reduces the number of oligonucleotide sequences in said virtual library of oligonucleotide sequences by one or more of i) a process of selection based on target accessibility to said selected nucleic acid, ii) a process of selection based on uniform distribution of oligonucleotide compounds across said selected nucleic acid, or iii) a process of selection based on targeting a functional region of said selected nucleic acid; wherein said computer system searches at least one database for alternative transcripts;~~

i) generates a list of oligonucleotide sequences according to a desired oligonucleotide length, thereby generating a series of oligonucleotide sequences, wherein said computer system

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searches at least one database for alternative transcripts for said selected nucleic acid;

ii) applies a virtual oligonucleotide chemistry to the oligonucleotide sequences generated in step i) to yield a set of virtual oligonucleotides;

iii) generates a subset of said set of virtual oligonucleotides based on: a) targeting a functional region of said selected nucleic acid, b) target accessibility to said selected nucleic acid, and/or c) uniform distribution of oligonucleotide compounds across said selected nucleic acid; and

iv) generates synthesis instructions in computer manipulable form for said oligonucleotide sequences in said subset of said set of virtual oligonucleotides;

an automated synthesizer that receives said synthesis instructions from said computer system and synthesizes only that set of real oligonucleotides that corresponds to said virtual set of oligonucleotide sequences consisting of said reduced number of oligonucleotide sequences said oligonucleotide sequences in said subset of said set of virtual oligonucleotides; and

an apparatus that accepts said set of real oligonucleotides and performs at least one procedure for each of said real oligonucleotides wherein said procedure identifies particular members of said set that modulate expression of said selected nucleic acid, wherein said procedure is computer controlled polymerase chain reaction or computer controlled enzyme-linked immunosorbent assay.